

CLAIMS

1. A method of screening for copy number of target nucleic acid sequences in a sample of genetic material (10), the method comprising introducing to the sample (10) a plurality of different genetic probes (14) suitable to hybridise with respective target sequences and all flanked by the same or substantially the same primer binding sites, subjecting the sample (10) to conditions favouring hybridisation of the probes (14) to their respective sequences, and amplification of sample-bound probes (14) using a pair of primers, wherein analysis of the respective amounts of amplified probe (14) provides for quantitative determination of the copy number of the respective nucleic acid sequences in the sample (10).
2. A method according to claim 1, characterised in that each probe (14) is distinguishable from the other(s), for example by having distinguishing mobility characteristics through a separating gel.
3. A method according to claim 1 or 2, characterised in that the plurality of different probes (14) comprises a predetermined set of different probes (14) each chosen to be specific for a respective target nucleic acid sequence.
4. A method according to claim 3, characterised in that the set comprises probes (14) suitable to screen a plurality of different nucleic acid sequences simultaneously or substantially simultaneously such that determination of the quantity of each probe product produced enables quantitative determination of the copy number of the respective sequences in the sample.
5. A method according to claim 4, characterised in that the polymerase chain reaction is used to determine the quantity of each probe product produced.
6. A method according to any of the preceding claims, characterised in that the method is used to screen sequences of different genes or different

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sequences within a gene, such as different exons in a eukaryotic gene.

7. A method according to any of the preceding claims, characterised in that the method is used to detect genetic alterations such as genetic deletions (reduction in sequence copy number) and genetic amplification (increase in sequence copy number).
8. A method according to any of the preceding claims, characterised in that the genetic material (10) is immobilised prior to hybridisation, such that hybridised flanking primers are likewise immobilised.
9. A method according to any of the preceding claims, characterised in that an excess of probes (14) is used.
10. A method according to any of the preceding claims, characterised in that probes (14) labelled for ready identification are used.
11. A method according to claim 10, characterised in that probes labelled with fluorescent labels are used.
12. A method according to any of claims 3 to 11, characterised in that more than one set of probes (14) is used, either simultaneously or sequentially.
13. A method according to claim 12, characterised in that the flanking primer pairs are the same for each set of probes (14).
14. A method according to claim 12, characterised in that the flanking primer pairs are different for each set of probes (14).
15. A method according to any of the preceding claims, characterised in that the method comprises means to obviate or mitigate hybridisation between primer binding sequences.

16. A method according to claim 15, characterised in that competing oligonucleotides are introduced to the sample preferably during the hybridisation stage to releasably bind to the primer binding sites flanking each probe whereby to mitigate primer binding site interactions.
17. A method according to any of the preceding claims, characterised in that unbound probes (14) and primers are thoroughly washed away from the bound probes (14) following hybridisation stage and prior to analysis.
18. A method according to any of claims 3 to 17, characterised in that the method is used to screen DNA, RNA and/or cDNA with appropriate probe sets.
19. A method according to claim 18, characterised in that the method is used to screen somatic and/or germline sequences.
20. A method according to claim 18 or 19, characterised in that the method is used to screen for polymorphic alterations.
21. A set of probes (14) substantially as described above in any of the preceding claims.
22. A kit for such a method described above in any of the preceding claims, which kit comprises a probe set (14) generally as defined above, amplification primers and means to enable amplification and analysis of amplification product(s).
23. A method of screening for copy number of target nucleic acid sequences in a sample of genetic material substantially as hereinbefore described with reference to the accompanying examples and drawings.
24. A set of probes substantially as hereinbefore described with reference to the accompanying examples and drawings.

25. A kit for a method of screening for copy number of target nucleic acid sequences in a sample of genetic material substantially as hereinbefore described with reference to the accompanying examples and drawings.

26. Any novel subject matter or combination including novel subject matter disclosed herein, whether or not within the scope of or relating to the same invention as any of the preceding claims.

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